

Supplementary Figure & Tables

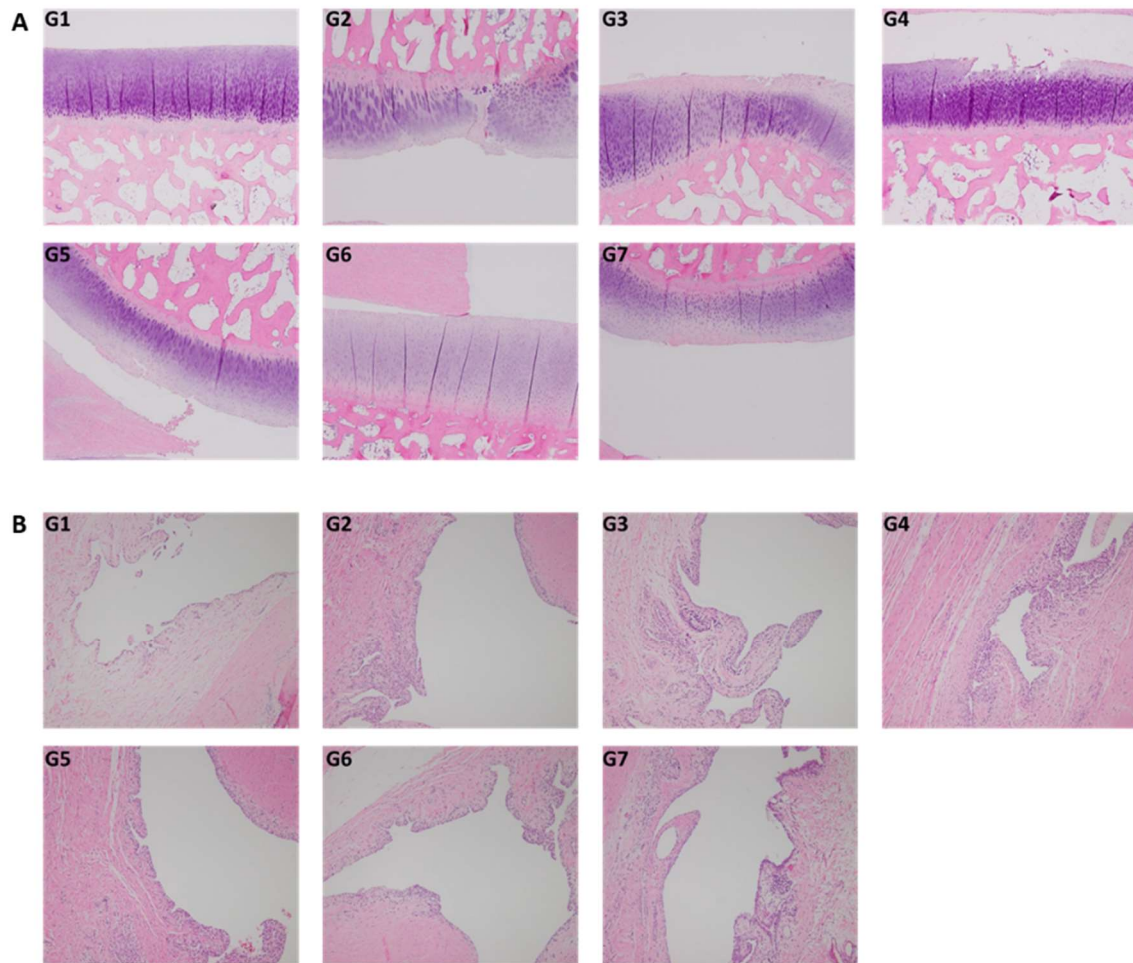


Figure S1. The results of histological examination in a canine model of OA. The paraffin-embedded tissue slides of cartilage or synovium were stained with H&E dye. For microscopic examination, a magnification of X40 was utilized for (A) cartilage, while a magnification of X100 was employed for (B) synovium. The total cartilage score and total synovial score were quantified and subsequently incorporated into the OARSI score. Data are expressed as Mean \pm S.D. Day of first test article administration was designated day 0. G1: Normal control, G2: Vehicle control, G3: Positive control, G4: 200 mg IR, G5: 300 mg IR, G6: 300 mg MR, G7: CR-1

Table S1. The criteria of gait evaluation.

Score	Parameters
0	No observable lameness
1	Intermittent, mild weight-bearing lameness with little, if any, change in gait
2	Moderate weight-bearing lameness—obvious lameness with noticeable gait change
3	Severe weight-bearing lameness— “toe-touching” only
4	Non-weight-bearing

Table S2. Grading of cartilage structure.

Severity of Pathology Characteristics		Area of Section Affected			
		None	Local (Approx 1/3)	Multi-Focal (Approx 2/3)	Global (>2/3)
A	Normal volume, smooth surface with all zones intact	0	0	0	0
B	Surface undulations including fissures in surface/upper zone and/or pannus tissue formation on surface	0	1	2	3
C	Fissures to mid-zone and/or erosion of surface/upper zone	0	2	4	6
D	Fissures that extend to deep zone and/or erosion through mid-zone	0	3	6	9
E	Full thickness loss of cartilage	0	4	8	12

Table S3. Grading of chondrocyte pathology.

Severity of Pathology Characteristics		Area of Section Affected			
		None	Local (Approx 1/3)	Multi-Focal (Approx 2/3)	Global (>2/3)
A	Normal	0	0	0	0
B	Loss of cells in the surface zone or relative increased density with occasional superficial clusters	0	1	2	3
C	Small cell clusters (2–4 cells/cluster) predominate	0	2	4	6
D	Large cell clusters (≥ 5 cells/cluster) predominate	0	3	6	9
E	Cell loss (necrosis/apoptosis) predominates	0	4	8	12

Table S4. Grading of proteoglycan staining.

Severity of Pathology Characteristics		Area of Section Affected			
		None	Local (Approx 1/3)	Multi-Focal (Approx 2/3)	Global (>2/3)
A	Normal	0	0	0	0
B	Decreased proteoglycan content in surface/upper zone	0	1	2	3
C	Decreased proteoglycan content into the mid-zone	0	2	4	6
D	Decreased proteoglycan content into the deep zone	0	3	6	9
E	Full depth decrease in proteoglycan content	0	4	8	12

Table S5. Grading of lining cells characteristics.

Severity of Pathology Characteristics		Area of Section Affected			
		None	Local (Approx 1/3)	Multi-Focal (Approx 2/3)	Global (>2/3)
A	1–2 layers of cells	0	0	0	0
B	3–6 layers of cells	0	1	2	3
C	>6 layers of cells	0	2	4	6

Table S6. Grading of cell infiltration characteristics.

Severity of Pathology Characteristics		Area of Section Affected			
		None	Local (Approx 1/3)	Multi-Focal (Approx 2/3)	Global (>2/3)
A	No cellular infiltration	0	0	0	0
B	Mild to moderate inflammatory cell infiltrates including small lymphoid follicles	0	1	2	3
C	Marked, diffuse inflammatory cell infiltrates including large lymphoid follicles	0	2	4	6

Table S7. Grading of hyperplasia characteristics.

Severity of Pathology Characteristics		Area of Section Affected			
		None	Local (Approx 1/3)	Multi-Focal (Approx 2/3)	Global (>2/3)
A	No villous hyperplasia	0	0	0	0
B	Short villi	0	1	2	3
C	Finger-like hyperplasia	0	2	4	6